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Larson & Anderson, LLC			HADDAD, MAHER M	
re: MSK				
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

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RESPONSE TO APPLICANT'S AMENDMENT

1. Applicant's amendment, filed 11/13/09, is acknowledged.
2. Claims 1-3, 5-10 and 15-22 are pending.
3. Claims 6, 10, 16, 18 and 20 stand withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to a nonelected invention.
4. Claims 1-3, 5, 7-9, 15, 17, 19 and 21-22 are under consideration in the instant application a method for inhibition of pathological angiogenesis in a tissue prone to pathological angiogenesis and expressing $\alpha 6\beta 4$ integrin, comprising the steps of exposing the tissue to a therapeutic agent effective to reduce the amount of active $\alpha 6\beta 4$ integrin in the tissue, wherein the therapeutic agent targets and inhibits the signaling function of $\beta 4$, thereby inhibiting pathological angiogenesis.
5. The following new ground of rejections are necessitated by the amendment submitted 11/13/09.
6. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

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7. Claims 1-3, 5, 7-9, 15, 17, 19 and 21-22 stand provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-4, 6, 14-20 and 23-24 of copending Application No. 10/596,364. Although the conflicting claims are not identical, they are not patentably distinct from each other because both applications use inhibitors of $\alpha 6\beta 4$ integrin that target $\beta 4$ as therapeutic agents to inhibit tumorigenesis in individuals, including humans, of tumors that express $\alpha 6\beta 4$ integrin, wherein the agent is antibody.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Applicant's arguments, filed 1/13/09, have been fully considered, but have not been found convincing.

Applicants point out that the claims of this application are directed to inhibition of angiogenesis, not inhibition of initiation of primary or metastatic tumor growth as in the cited application. The Examiner has not addressed the differences in the claims in making this rejection, and indeed erroneously states that the claims are all directed to inhibition of tumorigenesis.

However, it remains the Examiner's position while the preamble of the conflicting claims are different however, the same product is used in the method with same method steps and patient populations, therefore the practice of the invention of '364 application would necessarily result in the practice of the instant invention and vice versa.

Furthermore, Applicants challenge the authority of the US Patent and Trademark Office, and administrative agency, to apply a rule developed in equity by the Courts. Nothing in the treatment of this rule by the Patent and Trademark Office considers equitable principles, nor is an administrative agency empowered to act in equity outside of the guidelines of properly promulgated regulations. There are no laws or regulations relating to the standards for obviousness-type double patenting and therefore in making this rejection the Patent Examiner and the Patent and Trademark Office are exceeding their authority.

However, the Examiner has no authority to comment on the legality of the rules, guidelines and regulations.

In rejecting the claims of this application under both § 112, first paragraph and § 103, the Examiner has argued that the Examples in the specification are presumed not to have the stated characteristics, whilst compositions are the cited art are presumed to have these characteristics. There is no technical argument made to justify this differential treatment of antibodies. Applicants respectfully invite the Examiner to choose one position, and to support it with substantiated reasoning and to drop the rejection that is inconsistent with what the examiner chooses to perceive as based on supportable assertions.

However, the previous Office Action, mailed 5/13/09, has no dual rejections under § 112, first paragraph, enablement, and § 103, it is not clear what inherent inconsistency in the Examiner's position Applicant is referring to. Further, the specification do not appear to add anything further to the teachings of the prior art, if the specification is enabling, the prior art is also

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enabling, and if the prior art is not enabling, neither is the specification. The burden is thus placed on applicant, and properly so, to point out how the teachings of the specification go beyond those of the prior art.

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 1-3, 5, 7-9, 15, 17, 19 21 and 22 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for the same reasons set forth in the previous Office Action mailed 5/13/09.

Applicant's arguments, filed 1/13/09, have been fully considered, but have not been found convincing.

Applicant submits that the standards set forth by the Examiner are permissive ways in which written description **may** be satisfied, but they are not mandatory. The examiner has offered no clear statement apart from "not enough examples" as to why a person skilled in the art would not recognize the inventors as having possession of the claimed invention. See also Example 12 in the Training Materials at <http://www.uspto.gov/web/menu/written.pdf>.

However, there is no described or art-recognized correlation or relationship between the structure of the invention, the therapeutic agent which targets and inhibits the signaling function of $\beta 4$ and its inhibition of pathological angiogenesis function, the feature deemed essential to the instant invention. Therefore, one of skill in the art would not envisage, based on the instant disclosure, the claimed genus of therapeutic agent which targets and inhibits the signaling function of $\beta 4$ which retain the features essential to the instant invention.

Applicant contends that the examiner has not explained what it is about the Sepp article that he believes (sic, believes) justifies this conclusion. The examiner has also not responded to Applicants (sic, Applicants) discussion of the reference:

Sepp merely discloses that use of two specific promoters of angiogenesis (bFGF and PMA) lead to a reduction of $\beta 4$. The Examiner's argument ignores cause and effect, as well as the many reasons $\beta 4$ may be reduced. The Examiner also ignores the statement that bFGF stimulation of bovine adrenal cortex endothelial cells induces an increase in $\beta 4$ production. Sepp, at 270. In addition, as the Examiner has pointed out, the two functions of $\beta 4$ -adhesion and signaling- are quite separate. It is entirely plausible both that reduction of $\beta 4$ adhesion would lead to angiogenesis and reduction of $\beta 4$ signaling would lead to antiangiogenesis. Sepp does not provide any information about which function of $\beta 4$ is reduced; it merely states that overall $\beta 4$ is reduced. The experimental data provided in the specification shows that inhibition of signaling does have an antiangiogenic effect. The present invention concerns a reduction in the amount of signaling function of $\beta 4$, not overall $\beta 4$.

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However, it remains the Examiner's position that Applicant did not describe the claimed "agent that targets and inhibits the signaling function of $\beta 4$ " sufficiently to show they had possession of the claimed genus of agent. It is the examiner's position that the prior art of Sepp et al teach that inhibiting the signaling function of $\beta 4$ does not lead to the inhibition of angiogenesis.

Accordingly, it is not clear that the listed human and mouse RNAi species and anti- $\beta 4$ antibodies would function as claimed. While the specification provides two anti- $\beta 4$ antibodies, however, they have not been show to inhibit $\beta 4$ integrin signaling.

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e1) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

35 U.S.C. § 102(e), as revised by the AIPA and H.R. 2215, applies to all qualifying references, except when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. For such patents, the prior art date is determined under 35 U.S.C. § 102(e) as it existed prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. § 102(e)).

11. Claims 1-3, 5, 7-9, 15, 17, 19 and 21-22 are rejected under 35 U.S.C. 102(e)/(b) as being anticipated by US 20030224993 (IDS reference)/WO 02/30465 for the same reasons set forth in the previous Office Action mailed 5/13/09.

Applicant's arguments, filed 1/13/09, have been fully considered, but have not been found convincing.

Applicant submits that the Examiner's argument fails to take into account that angiogenesis is something that occurs after a period of tumor growth, so that cells of a given cancer type may not be secreting agents to stimulate angiogenesis. In addition, the tissue in which a tumor is located may not be prone to angiogenesis even if the tumor is secreting such agents. There are no experiments described in Land (even prophetically) that would assess effect on angiogenesis. Thus, there is no basis to assume that anything concerning angiogenesis occurred inherently in Land.

However, the claims recites "inhibition of pathological angiogenesis in a tissue prone to pathological angiogenesis" the prior art cancer conditions are prone to pathological angiogenesis.

It is further pointed out that the Examiner is unfairly making unchallengeable allegations about the presumed qualities of the Land antibodies, since no specific antibodies are disclosed in Land in a manner which would permit comparative testing. Indeed, there is no indication in Land that any antibody was ever made.

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However, the claims are not limited to antibodies as applicant argues, the claims recite “therapeutic agent targets and inhibits the signaling function of $\beta 4$ ”. Land teaches agents such as antisense molecules to beta4 mRNA (see published claims 28-29 in particular). Regarding the antibody issue, the standard for what constitutes sufficient enablement of prior art reference for purpose of anticipation under 35 U.S.C. 102(b) differs from enablement standard under Section 112, in that the prior art reference need not demonstrate utility in order to serve as anticipating reference under Section 102. See *Rasmusson* at 1325 (“The standard for what constitutes proper enablement of a prior art reference for purposes of anticipation under section 102, however, differs from the enablement standard under section 112. In *In re Hafner*, 56 C.C.P.A. 1424, 410 F.2d 1403 (Cust. & Pat.App. 1969), the court stated that “a disclosure lacking a teaching of how to use a fully disclosed compound for a specific, substantial utility or of how to use for such purpose a compound produced by a fully disclosed process is, under the present state of the law, entirely adequate to anticipate a claim to either the product or the process and, at the same time, entirely inadequate to support the allowance of such a claim.” *Id.* at 1405; see *Schoenwald*, 964 F.2d at 1124; *In re Samour*, 571 F.2d 559, 563- 64 (Cust. & Pat.App. 1978).”)

Applicant submits that the Examiner seems to confusing the standards for patentability of compositions, which do not become patentable simply because a mechanisms of action is discovered, and patentability of method claims. The present claims are method claims, and the mechanism, scope and nature of the activity is highly relevant to how a composition is used, making method claims patentable even for old compositions.

It appears that applicant and the examiner differ on interpretation of both the claimed methods and the prior art. Also, applicant relies upon an asserted and claimed mechanism of action but does not provide objective evidence that the prior art teaching of treating the same cancer patient populations with the same compositions to achieve the same therapeutic effect differs from the claimed methods.

12. Claims 1-3, 5, 7-9, 15, 17, 19 and 21-22 stand rejected under 35 U.S.C. 102(b) as being anticipated by Abdel-Ghany et al (JBC, 276(27):25438-25446, 2001) (IDS reference) for the same reasons set forth in the previous Office Action mailed 5/13/09.

Applicant’s arguments, filed 1/13/09, have been fully considered, but have not been found convincing.

Applicant submits that Abdel-Ghany, like Land, is silent with respect to angiogenesis, and indeed focuses on adhesion (i.e., binding) of cancer cells by binding a newly identified ligand, hCLCA2, to $\beta 4$. There is no discussion of signaling function, and the only use of antibodies is to confirm binding affinity.

However, the mechanism of action does not have a bearing on the patentability of the invention if the invention was already known or obvious. Even though applicant has proposed or claimed the mechanism by which anti- $\beta 4$ antibodies inhibit pathological angiogenesis of tumor does not appear to distinguish the prior art teaching the same methods to achieve the same end-results. Mere recognition of latent properties in the prior art does not render nonobvious an otherwise known invention. *In re Wiseman*, 201 USPQ 658 (CCPA 1979). Granting a patent on the

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discovery of an unknown but inherent function would remove from the public that which is in the public domain by virtue of its inclusion in, or obviousness from, the prior art. *In re Baxter Travenol Labs*, 21 USPQ2d 1281 (Fed. Cir. 1991). See M.P.E.P. 2145.

13. No claim is allowed.

14. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad whose telephone number is (571) 272-0845. The examiner can normally be reached Monday through Friday from 7:30 am to 4:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

November 20, 2009

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